REMARKS

Applicant, through the undersigned, wishes to thank Examiner Woitach for the courtesy and assistance extended on behalf of Applicants during a personal interview conducted on April 21, 2005.

In the Final Action dated November 29, 2004, claims 50-67 are pending and under consideration. Claims 50-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting, as allegedly unpatentable over claims 13-15 and 20 of copending application, Serial No. 09/670,198. Claims 50-56 and 59-65 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. Claims 57-58 and 66-67 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Thomson (US Patent 5,843,780). Claims 57-58 and 66-67 are also rejected under 35 U.S.C. §102(e) as allegedly anticipated by Carpenter et al. (US 2002/0019046 A1). Further, the Examiner has objected to the Abstract of the application.

This Response addresses each of the Examiner's rejections and objections. Applicant therefore respectfully submits that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Applicant first respectfully submits that an amended Abstract was provided in Applicant's Response dated December 4, 2003, and was acknowledged by the Examiner in the Office Action dated March 9, 2004. Accordingly, the objection to the Abstract is overcome and withdrawal thereof is respectfully requested.

With respect to the claims, Applicant has amended claims 50 and 59 to recite a "method of producing a human neural progenitor cell" (hNPC), wherein the intermediate progenitor cell is cultured in "a neural progenitor culture medium" to differentiate into the neural

progenitor cell. Such amendment is supported by the specification, for example, page 15, lines 16-19, where the specification states that placement of the noggin treated cells in neural progenitor culture medium supports the differentiation of the cells towards neurospheres containing neural progenitor cells. Support for "a neural progenitor culture medium" is also found in the specification, e.g., on page 14, line 30 to page 15, line 10; page 16, line 4. Thus, an exposure to noggin directs the differentiation of the ES cells away from the undifferentiated state, and as stated in the specification, the noggin-treated cells are capable of undergoing commitment of neurogenic lineages. No new matter is introduced by the amendments to claims 50 and 59.

Applicant has also added claim 68, which depends from claims 50 and 59, to further define the ES cell marker that is not expressed in the progenitor cell as Oct 4 or cripto. Support for claim 68 is found in the specification, e.g., on page 28, lines 14-15.

New claims 69-79 are directed to a method of producing a human progenitor cell by culturing an undifferentiated human ES cell in the presence of an antagonist of a BMP mediated default pathway. These claims correspond to previous claims 50-56; however, the resulting progenitor cell is now defined as lacking at least one marker of said undifferentiated ES cell, lacking a marker of neuroectoderm, and capable of differentiating into said neural progenitor cell. Support for the present characterization of the progenitor cell is found in the specification, e.g., on page 15, lines 16-26; and page 28, lines 14-19.

New claims 80-83 are directed to progenitor cells prepared according to the method of claim 69-78. In light of new claims 80-83, claims 57-58 and 66-67 have been canceled without prejudice.

Applicant respectfully submits that the foregoing amendments do not introduce new matter.

In the Final Action, the Examiner indicates that claims 50-67 broadly encompass any species of BMP antagonist. The Examiner states that the claims are examined to the extent that they encompass the elected species of noggin. Applicant respectfully reminds the Examiner that, as indicated in the Office Action dated February 25, 2003, Applicant shall be entitled to consideration of claims to additional species that are written in dependent form or otherwise include all the limitations of an allowed generic claim, once the generic claim is found allowable.

Claims 50-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting, as allegedly unpatentable over claims 13-15 and 20 of copending application, Serial No. 09/670,198. The Examiner contends that, although the conflicting claims are not identical, they are not patentably distinct from each other, because in each case the claims are drawn to methods of culturing comprising the same steps and using noggin as an antagonist/inhibitor of the BMP pathway.

Applicant assumes that the Examiner intended to reference Serial No. 10/616,682, which is a continuation application of Serial No. 09/670,198, as Serial No. 09/670,198 is abandoned. See the Office Action dated March 9, 2004. Applicant also observes that claim 13 of the '682 application is drawn to a method that involves culturing a pluripotent cell line in the presence of an inhibitory factor of BMP-2, wherein the pluripotent cell can be human embryonic stem (ES) or human embryonic germ (EG) cells (claims 14-15), and wherein the inhibitory factor can be noggin (claim 20). Therefore, Applicant will address the rejection as if the rejection is based on claims 13-15 and 20 of Serial No. 10/616,682.

Applicant respectfully submits that claims 50-56, 59-65 and 68, as presently amended, are directed to methods of producing neural progenitor cells. As written, claims 13-15 and 20 of the '682 application are directed to methods of "regulating growth and/or differentiation of pluripotential cells". It is observed that the '682 application is not at all directed to neural progenitor cells or the preparation thereof. The applicant of the '682 application characterizes the invention therein as based on the discovery that BMP-2 induces differentiation of human pluripotent cells (specifically, human EC cells) into a cell type with the properties of extraembryonic endoderm. See Paragraph 0011 of the '682 application. Thus, the '682 application proposes to utilize a BMP-2 inhibitor to support stem cell renewal and/or limit extraembryonic differentiation. For example, the '682 application states that a BMP-2 antagonist should be used at a dose determined to inhibit extraembryonic differentiation. See Paragraph 0025 of the '682 application. Claims 13-15 and 20 are understood to be methods of promoting stem cell renewal or limiting extraembryonic differentiation. In contrast, claims 50-56, 59-65 and 68 of the present invention are drawn to methods of differentiating a human ES cell into a neural progenitor cell. Thus, Applicant respectfully submits that claims 50-56, 59-65 and 68 of the present invention are clearly patentably distinct over claims 13-15 and 20 of the '682 application.

Applicant further submits that new claims 69-83 are also patentably distinct over claims 13-15 and 20 of the '682 application. Claims 69-83 are drawn to methods of producing a human progenitor cell by culturing an undifferentiated human ES cell in the presence of an antagonist of a BMP mediated default pathway, as well as the progenitor cell produced thereby. The progenitor cell, which is an intermediate cell type, is defined in the claims as lacking at least one marker of the undifferentiated ES cell, lacking a marker of neuroectoderm, and capable of

differentiating into a neural progenitor cell. This capacity of the progenitor cell to undergo commitment to a neural lineage, as well as the culture conditions to differentiate a human ES cell to obtain such progenitor cell, are uniquely recognized by the present inventors.

In contrast, claims 13-15 and 20 of the '682 application are drawn to methods of "regulating growth and/or differentiation of pluripotential cells". As submitted above, claims 13-15 and 20 of the '682 application are understood to be methods of promoting stem cell renewal or limiting extraembryonic differentiation. The claims of the '682 application are not at all directed to differentiation of a pluripotent cell to an intermediate cell type as presently characterized in claims 69-83. As broadly characterized by claims 13-15 and 20 of the '682 application, the resulting cell can be a cell which continues to grow in a pluripotent state without differentiating into an extraembryonic lineage – that is, the resulting cell would not lack at least one expression marker of the undifferentiated ES cell. The '682 application is not directed to obtaining or identification of a progenitor cell as characterized in the present claims.

Accordingly, Applicant respectfully submits that claims 69-83, drawn to methods that differentiate a human ES cell into a progenitor cell capable of giving rise to neural cell types, are also patentably distinct from claims 13-15 and 20 of the '682 application.

Further, it is observed that the examples provided in the '682 application, specifically, Examples 1-4, are all related to the effects of BMP on a human pluripotent cell. There is no exemplification of the effect of a BMP inhibitor on a human pluripotent cell. Moreover, the examples provided in the '682 application are all related to cultures of embryonic carcinoma (EC) cells. EC cells are generally karyotypically abnormal (i.e., these cells generally do not carry a normal complement of chromosomes), and have different physical characteristics and

differentiation profiles relative to ES cells or EG cells. There is no exemplification in the '682 application relating to cultures of ES or EG cells.

Applicant respectfully submits that the instant double patenting rejection is a provisional rejection, as the '682 application has not issued. It is respectfully submitted that the rejection is premature under the present circumstance where the claims of the present application are rejected over the unexamined claims of a published application. In any event, Applicant respectfully submits the present claims are patentably distinct over claims 13-15 and 20 of the '682 application.

In view of the foregoing, it is respectfully submitted that the double patenting rejection based on claims 13-15 and 20 of the '682 application is overcome. Withdrawal of the rejection is therefore respectfully requested.

Claims 50-56 and 59-65 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

The Examiner acknowledges that the specification is enabling for methods of culturing human embryonic stem (ES) cells comprising obtaining a source of human ES cells, and culturing the human ES cells in the presence of noggin for five days, thereby resulting in an intermediate cell type which does not express ES stem cell markers. The Examiner also acknowledges that the specification teaches that such intermediate cell type can be used to produce neural progenitor cells. However, the Examiner alleges that the specification does not provide enablement for methods of producing any progenitor cells as claimed.

Applicant respectfully submits that new claims 69-79 are directed to a method of producing a human progenitor cell by culturing an undifferentiated human ES cell in the presence of an antagonist of a BMP mediated default pathway. These claims correspond to

previous claims 50-56; however, the resulting progenitor cell is further defined as lacking at least one marker of the undifferentiated ES cell, lacking a marker of neuroectoderm, and capable of differentiating into a neural progenitor cell. This delineation is intended to clarify the nature of the progenitor cell as an intermediate cell type.

Applicant respectfully submits that the specification provides ample guidance for the production of such an intermediate cell type by using a BMP antagonist such as noggin. The specification has also provided examples to illustrate the antagonists (e.g., noggin), the appropriate concentrations of the antagonist, and the time period of culture, which are appropriate for use in the claimed methods. See 27-29 of the specification.

Furthermore, Applicant respectfully submits that the specification also provides clear teaching to allow those skilled in the art to determine whether the intermediate cell type has been produced from hES cells. For example, the specification describes that cells of the intermediate cell type form colonies consisting of distinct small round cells and differ in appearance from ES cells (see page 13, lines 11-24). The specification also describes the presence or absence of certain expression markers that would facilitate the identification of the intermediate cell type (see page 13, line 20 to page 14, line 5; page 28, lines 14-19).

Accordingly, it is respectfully submitted that claims 69-79, drawn to methods of producing a progenitor cell from a hES cell, are fully enabled by the specification.

Moreover, with respect to claims 50-56, 59-65 and 68, the claims are presently directed to methods of producing human neural progenitor cells. As submitted hereinabove and acknowledged by the Examiner, such claimed methods are disclosed in the specification, for example, page 15, lines 16-19; and page 27-29.

Applicant respectfully submits that the instant amendment has fully addressed the Examiner's concern with respect to the types of progenitors that can be produced by the claimed methods. As such, it is respectfully submitted that the enablement rejection under 35 U.S.C. §112, first paragraph, is overcome and withdrawal thereof is requested.

Claims 57-58 and 66-67 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Thomson (US Patent 5,843,780).

The Examiner alleges that the recitation in the claims that defines the progenitor cell as "lacking at least one marker of an undifferentiated ES cell", is not supported by the specification. Thus, the Examiner states that the claims are given their broadest reasonable interpretation. Because Thomson teaches primate embryonic stem cells, the Examiner contends that such ES cells are capable of giving rise to the various somatic cell lineages and would therefore be considered "progenitor" cells. Thus, the Examiner concludes that Thomson anticipates the claimed progenitor cells.

In the first instance, Applicant respectfully submits that claims 57-58 and 66-67 have been canceled in light of newly added claims 80-83. New claims 80-83 are directed to human progenitor cells prepared by culturing a hES cell in the presence of a BMP antagonist.

Applicant respectfully submits that Thomson only teaches primate embryonic stem cells and spontaneous differentiation of those cells. Thomson has only illustrated the use of cells originated from non-human primates, namely the common marmoset and the rhesus monkey. In contrast, the presently claimed progenitor cells (claims 78-80) are human progenitor cells.

Furthermore, it is also clear from the specification that the claimed human progenitor cells are distinct from hES cells, since they differ in appearance from hES cells (page 13, line 13) and lack markers of hES cells. The specification also demonstrates that the progenitor cells lack

Oct-4 or cripto expression (page 28, line 15), both of which are markers expressed by hES cells. Additionally, the expression of GCTM-2, a stem cell marker (or the proportion of cells expressing GCTM-2), is also reduced in the instant progenitor cell or cell population. See, e.g., page 27, lines 25-27. In light of the instant disclosure, it is clear that the progenitor cells presently claimed do not necessarily lack all markers of hES cells; and the specification has shown the production of progenitor cells lacking at least one marker of hES cells (Oct-4 or cripto).

Applicant acknowledges that the progenitor cell may not be fully characterized in all of its expression markers and properties. However, there is no requirement under the law for a complete characterization of a composition in order to obtain patentable protection. In the instance case, the progenitor cells, as presently claimed, are both defined by the manner in which they are prepared, by their lack of an expression marker of hES cells (indicating a distinct differentiation status relative to hES cells), and by their capacity to give rise to neural cell types yet lacking a marker of neuroectoderm. These features, in combination, sufficiently distinguish the progenitor cells as claimed from the pluripotent primate ES cells disclosed by Thomson.

In view of the foregoing, it is respectfully submitted that the rejection under 35 U.S.C. §102(b) based on Thomson is overcome.

Claims 57-58 and 66-67 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by Carpenter (US 2002/0019046 A1).

It is observed that the Examiner has not disputed Applicant's assertion in the previous response that Carpenter's teaching, insofar as it relates to the use of noggin in culturing hES cells in order to obtain a progenitor cell, is absent in Carpenters priority documents and only appears in the application filed on June 21, 2001, i.e., after the priority date of the present application.

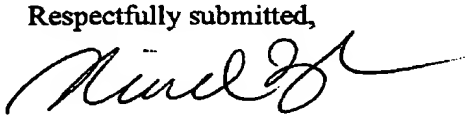
The Examiner's rejection is allegedly based on the teaching by Carpenter of human embryonic stem cells that, in the Examiner's opinion, are progenitor cells that are within the scope of the present claims.

As submitted above, the human progenitor cells as claimed in claims 80-83 are distinct from hES cells, since they differ in appearance from hES cells (page 13, line 13) and lack at least one marker of hES cells. Therefore, the progenitor cells of claims 80-83 are not anticipated by Carpenter.

Accordingly, the rejection based on Carpenter under 35 U.S.C.§102(e) is overcome. Withdrawal of the rejection is therefore respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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